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| 10/528,846 | 02/09/2006 | Tatsuo Hoshino | 21414 US C0381435/0186340 | 2015 |
| 7590 Stephen M Haracz Bryan Cave 1290 Avenue of the Americas New York, NY 10104 | | | EXAMINER CHOWDHURY, IQBAL HOSSAIN | |
| | | | ART UNIT 1652 | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/528,846

Applicant(s)

HOSHINO ET AL.

Examiner

Iqbal H. Chowdhury, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2 and 4-8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2, 4-8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Application Status

In response to a previous Office action, a non-final requirement (mailed on 12/5/2006), Applicants filed a response and amendment received on 5/10/2007, amending claims 1-2, and 4-7, canceling claim 3, and adding new claim 8 is acknowledged.

Claims 1-2, and 4-8 are under consideration and will be examined herein.

Applicants' arguments filed on 5/10/2007, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Maintained- Claims Rejections- 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Previous rejection of Claims 1-2, and 4-7 under 35 U.S.C. 103(a) as being unpatentable over Misawa et al. (GenBank Accession No. D58422, *Alcaligenes* sp. crtW and crtZ genes for beta-carotene hydroxylase and beta-Carotene ketolase, complete cds, created on 7/22/1995) Misawa et al. (Canthaxanthin biosynthesis by the conversion of methylene to keto groups in a hydrocarbon beta-carotene by a single gene, *Biochem Biophys Res Commun.* 1995 Apr 26; 209(3): 867-76, see IDS) in view of Hoshino et al. (US Patent 6,365,386 B1, issue date 4/2/2002, see IDS) is maintained and newly added claim 8 is included in this rejection.

The instant claims are drawn to a process for producing canthaxanthin and echinenone, which comprises cultivating in an aqueous nutrient medium at a pH range of 4 to 8, temperature range of 15 to 26°C for 24 to 500 hrs, a recombinant *Xanthophyllomyces dendrorhous* (*Phaffia rhodozyma*) microorganism that comprises a polynucleotide sequence that encodes a β -carotene ketolase, wherein β -carotene accumulates in the medium under aerobic conditions, and isolating carotenoids from the recombinant microorganism or from the medium, wherein the polynucleotide sequence is originated from a microorganism which is selected from the group

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consisting of *Agrobacterium aurantiacum*, *Alcaligenes* PC-1, *Paracoccus marcusii* MH1, a gram-negative bacteria E-396 (FERM BP-4283), and *Haematococcus pluvialis*.

Applicants in his lengthy arguments argue that claim 1 has been amended and therefore, not unpatentable over the prior art. Applicants also argue that the Examiner bears the burden to set forth a *prima facie* case of unpatentability and if the PTO fails to meet its burden, then the applicant is entitled to a patent and thus, the rejection is legally deficient and should be withdrawn for this reason alone. Furthermore, Applicants argue that the rejection is also factually insufficient to support a rejection under § 103(a) and the obviousness cannot be based upon speculation, nor can obviousness be based upon possibilities or probabilities, and obviousness *must* be based upon facts. Applicants also argue that the rejection is also devoid of any discussion of the dependent claims. Accordingly, the record is devoid of any evidence that the Examiner individually considered the dependent claims. Accordingly, the rejection is also both factually and legally deficient as to the dependent claims. For this additional reason, the rejection should be withdrawn as to the dependent claims. Applicants also argue that the § 103 rejection is inconsistent with the enablement rejection, wherein in the enablement rejection, the Examiner asserts that the specification does not enable producing canthaxanthin and echinenone by using *any beta* carotene ketolase gene from *any* source, but, in seeking to combine Misawa I and Misawa II, the Examiner ignores his criticisms of the present specification, and if the § 103 rejection is legally sound, then the enablement rejection is not.

Applicant's amendments, and arguments have been fully considered but are not deemed persuasive to overcome the rejection on obviousness issues.

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Summarizing, what are claimed, 1) a process for producing canthaxanthin/echinenone, which is intermediate of astaxanthin biosynthesis from beta-carotene; 2) by using a microorganism *Xanthophyllomyces dendrorhous* (*Phaffia rhodozyma*) comprising a gene encoding beta-carotene ketolase gene of crtW from a *Alcaligenes* PC-1 in aerobic condition; 3) cultured the microorganism at pH 4-8, temperature 15-26oC for 24-500 hrs.

Summarizing, the teachings of prior art, 1) Misawa I (GenBank) teach a gene encoding beta-carotene ketolase of crtW from a *Alcaligenes* PC-1, which is 100% identical to instant application beta carotene ketolase gene; 2) Misawa II (BBRC), teach a process for producing canthaxanthin/echinenone by using a transformed *E. coli* comprising a gene encoding beta-carotene ketolase of crtW from a *Alcaligenes* PC-1, which is 100% identical to instant application beta carotene ketolase gene, wherein the cells are cultured at 28oC at a pH in which *E. coli* grows well i.e. pH 7-8 (which is well known in the art); and 3) Hoshino et al. teach a process for producing astaxanthin from beta-carotene in *Phaffia rhodozyma* (same strain used by the instant application) comprising beta-carotene ketolase (crtW), which produces canthaxanthin from beta-carotene and crtZ gene encoding an enzyme which converts canthaxanthin to astaxanthin by cultivating said microorganism at 20oC for overnight (i.e. 24 hr). The three prior arts clearly taught all the limitation including said method of producing canthaxanthin.

Since, Misawa et al. (BBRC) teach the whole process of the claimed invention except using *Phaffia rhodozyma*, for producing canthaxanthin from beta-carotene comprising beta-carotene ketolase of crtW from a *Alcaligenes* PC-1, therefore, one of ordinary skill in the art would have been motivated to use *Phaffia rhodozyma* instead of *E. coli* as taught by Hoshino et al. to produce canthaxanthin and echinenone because *Phaffia*, red yeast usually used for the

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microbiological production systems for natural astaxanthin, which comprises sufficient amount of natural substrate beta-carotene.

Therefore, It would have been obvious to one of ordinary skill in the art at the time of the invention was made to combine the teaching of Misawa et al. (GenBank), Misawa et al. (BBRC) and Hoshino et al. to produce canthaxanthin and echinenone from beta-carotene by using the beta-carotene ketolase gene (crtW) of Misawa et al. (GenBank) to transform the *Phaffia rhodozyma* of Hoshino et al. to produce canthaxanthin and echinenone by using the methods of Hoshino et al., which is the claimed method of the instant application. One of ordinary skill in the art would have a reasonable expectation of success because using recombinant *Phaffia rhodozyma* for producing canthaxanthin and echinenone is customary and widely used in the art for the biosynthesis of xanthophylls such as canthaxanthin, echinenone, astaxanthin and zeaxanthin from beta-carotene.

Thus, for the reasons above and as discussed previous office action, the rejection is maintained.

Regarding, inconsistency of 112 (1st) and 103 rejection, before amendments, claims 1-7 were rejected for Written description and scope of enablement because of lack of structural feature to correlate structure and function relationship and how to make and use the full scope of claimed genus in the methods of the claim. The 103 rejection was based on three prior arts, which disclose all the limitations of the portions of the claims which was previously deemed enabled and describe with proper motivation. Therefore, there was no inconsistency between the rejections.

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Conclusion

No claim is in condition for allowance.

Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution. **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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